## **Appendix 1: Supplementary tables** [posted as supplied by author]

Table A. Clinical features of a family cluster of two patients with novel avian influenza A (H7N9) virus infection in Eastern China, 2013

|   | Case two                   | Index case                 |  |  |
|---|----------------------------|----------------------------|--|--|
| General   |                            |                            |  |  |
| Age(years) and sex                                      | 32, female                 | 60, male                   |  |  |
| Temperature(°C)*  | $39.6~(~40.4^{\dagger}~)$  | $39.0~(40.2^{\dagger})$    |  |  |
| Day of onset  | March 21                   | March 8                    |  |  |
| Blood counts* White blood cells(×10 <sup>9</sup> per L) | 2.0 (0.4 <sup>‡</sup> )    | 5.9 (1.9 <sup>‡</sup> )    |  |  |
| Lymphocytes(×10 <sup>9</sup> per L)                     | $0.7(0.1^{\ddagger})$      | $0.3~(0.13^{\ddagger})$    |  |  |
| Platelets(×10 <sup>9</sup> per L)                       | 84 ( 77 <sup>‡</sup> )     | 120 (24 <sup>‡</sup> )     |  |  |
| Serum biochemistry*                                     |                            |                            |  |  |
| Alanine aminotransferase(U/L)                           | NA ( 96 <sup>†</sup> )     | 65 ( 181 <sup>†</sup> )    |  |  |
| Aspartate aminotransferase(U/L)                         | NA ( $203^{\dagger}$ )     | $148$ ( $178^{\dagger}$ )  |  |  |
| Albumin(U/L)  | $34.8 (25.4^{\ddagger})$   | 27.8 ( 24.1 <sup>‡</sup> ) |  |  |
| Creatinine(U/L)   | $62.7 \ (103.8^{\dagger})$ | 67.5 (102 <sup>†</sup> )   |  |  |
| Creatine kinase (U/L)                                   | NA (1063 <sup>†</sup> )    | NA                         |  |  |
| Lactate dehydrogenase (U/L)                             | NA (1291 <sup>†</sup> )    | NA (707 <sup>†</sup> )     |  |  |
| Coagulation*  |                            |                            |  |  |
| Prothrombin time (seconds)                              | 11.0 (16.6 <sup>†</sup> )  | NA (25.8 <sup>†</sup> )    |  |  |
| Activated partial thromboplastintime (seconds)          | $38.5 (60.7^{\dagger})$    | NA (59.2 <sup>†</sup> )    |  |  |
| Fibrinogen (g/L)  | $2.11 (5.18^{\dagger})$    | NA $(4.64^{\dagger})$      |  |  |
| Arterial blood*   |                            |                            |  |  |
| PaCO <sub>2</sub> (mm Hg)                               | 26 (31 <sup>‡</sup> )      | 23.4 ( 23.4 <sup>‡</sup> ) |  |  |
| PaO <sub>2</sub> (mm Hg)                                | 77 (18 <sup>‡</sup> )      | 54 ( 31 <sup>‡</sup> )     |  |  |
| Bicarbonate (mEq/L)                                     | 25.4 ( 12.5‡ )             | 16.3 ( 16.3 <sup>‡</sup> ) |  |  |
| Alveolar-arterial oxygen gradient (mm Hg)               | 29 (45 <sup>‡</sup> )      | NA (380 <sup>‡</sup> )     |  |  |
| Other   |                            |                            |  |  |
| Chest radiography                                       | Left side pneumonia        | Left side pneumonia        |  |  |

| Complications                         | ARDS, type I respiratory failure | ARDS, type I respiratory failure |  |
|---------------------------------------|----------------------------------|----------------------------------|--|
| Treatment                             |                                  |                                  |  |
| Mechanical ventilation                | Yes                              | Yes                              |  |
| Corticosteroids                       | Yes                              | Yes                              |  |
| Oseltamivir (75 mg/time, twice a day) | Yes (Started Mar. 19)            | Yes (Started Mar. 24)            |  |
| Passive immunotherapy                 | Yes                              | Yes                              |  |
| Outcome                               | Death                            | Death                            |  |
| Days from onset to death ordischarge  | 35                               | 57                               |  |
| Results of HI assay                   |                                  |                                  |  |
|                                       | 1:20 (March 29)                  | 1:320 (March 31)                 |  |
|                                       | 1:320 (April 17)                 | 1:320 (April 14)                 |  |

<sup>\*</sup>Data were measurement at admission and the values in the parentheses were the peak (denoted by  $\dagger$ ) or nadir (denoted by  $\ddagger$ ) measurement during hospitalization.

Table B. Detailed information of the 39 healthcare workers close contacts of the two H7N9 cases, Eastern China, 2013

| No. of close | Hospital | Department        | Occupation | Index<br>Case/Case | Period of contact with cases |      |
|--------------|----------|-------------------|------------|--------------------|------------------------------|------|
| contacts     | •        | •                 | •          | Two                | Start                        | End  |
| 01           | В        | ICU               | Doctor     | I & T              | 3-29                         | 4-1  |
| 02           | В        | ICU               | Nurse      | I & T              | 3-29                         | 3-30 |
| 03           | В        | ICU               | Nurse      | I & T              | 3-29                         | 3-29 |
| 04           | В        | ICU               | Nurse      | I & T              | 4-1                          | 4-1  |
| 05           | В        | ICU               | Doctor     | I & T              | 4-1                          | 4-1  |
| 06           | В        | ICU               | Doctor     | I & T              | 3-30                         | 3-31 |
| 07           | В        | ICU               | Doctor     | I & T              | 3-30                         | 3-31 |
| 08           | В        | ICU               | Doctor     | I & T              | 3-29                         | 4-1  |
| 09           | В        | ICU               | Doctor     | I & T              | 3-29                         | 4-1  |
| 10           | В        | ICU               | Doctor     | I & T              | 3-30                         | 3-31 |
| 11           | В        | PD                | Nurse      | T                  | 3-25                         | 3-31 |
| 12           | В        | PD                | Nurse      | T                  | 3-26                         | 3-28 |
| 13           | В        | PD                | Nurse      | T                  | 3-25                         | 3-27 |
| 14           | В        | PD                | Nurse      | T                  | 3-24                         | 3-28 |
| 15           | В        | PD                | Nurse      | T                  | 3-25                         | 3-28 |
| 16           | В        | PD                | Nurse      | T                  | 3-24                         | 3-28 |
| 17           | В        | PD                | Nurse      | T                  | 3-25                         | 3-28 |
| 18           | В        | PD                | Nurse      | T                  | 3-24                         | 3-27 |
| 19           | В        | PD                | Doctor     | T                  | 3-25                         | 3-28 |
| 20           | В        | PD                | Doctor     | T                  | 3-24                         | 3-28 |
| 21           | В        | PD                | Doctor     | T                  | 3-25                         | 3-28 |
| 22           | В        | PD                | Nurse      | T                  | 3-24                         | 3-26 |
| 23           | В        | PD                | Doctor     | T                  | 3-24                         | 3-26 |
| 24           | В        | Outpatient doctor | Doctor     | T                  | 3-21                         | 3-21 |
| 25           | A        | PD                | Nurse      | I                  | 3-11                         | 3-15 |
| 26           | A        | PD                | Nurse      | I                  | 3-11                         | 3-15 |
| 27           | A        | PD                | Doctor     | I                  | 3-11                         | 3-15 |
| 28           | A        | PD                | Doctor     | I                  | 3-11                         | 3-15 |
| 29           | A        | PD                | Doctor     | I                  | 3-11                         | 3-18 |
| 30           | A        | ICU               | Doctor     | I                  | 3-15                         | 3-18 |
| 31           | A        | ICU               | Nurse      | I                  | 3-15                         | 3-18 |
| 32           | A        | ICU               | Doctor     | I                  | 3-15                         | 3-18 |
| 33           | A        | ICU               | Nurse      | I                  | 3-15                         | 3-18 |
| 34           | A        | ICU               | Nurse      | I                  | 3-15                         | 3-18 |
| 35           | A        | ICU               | Nurse      | I                  | 3-15                         | 3-18 |
| 36           | A        | ICU               | Nurse      | I                  | 3-15                         | 3-18 |
| 37           | A        | ICU               | Nurse      | I                  | 3-15                         | 3-18 |
| 38           | A        | ICU               | Nurse      | I                  | 3-15                         | 3-18 |
| 39           | A        | PD                | Nurse      | I                  | 3-11                         | 3-15 |

Abbreviation: ICU- intensive care unit, PD - pneumology department, I - index case, and T- case two

Table C. Analysis of the key functional amino acid sites in different viral proteins associated with interspecies transmission or drug resistance of the three novel avian influenza A (H7N9) viruses related to a family cluster in Eastern China, 2013

| Protein* | Mutations responsible for viral phenotype change |       | Shanghai/1  | Shanghai/2 &<br>Anhui/1 | Nanjing/1   | Wuxi/1 <sup>&amp;</sup> | Wuxi/2 <sup>&amp;</sup> | Env/1 <sup>&amp;</sup> |
|----------|--|-------|-------------|-------------------------|-------------|-------------------------|-------------------------|------------------------|
| PB2      | Increased virulence in mice                      | Q591K | Q           | Q                       | K           | Q                       | Q                       | K                      |
|          | Associated with                                  | E627K | K           | K                       | Е           | K                       | K                       | Е                      |
|          | mammalian adaptation                             | D701N | D           | D                       | -           | D                       | D                       | D                      |
| PB1      | H5 virus transmissible among ferrets             | 1368V | I           | V                       | I           | V                       | V                       | I                      |
|          | Cleavage site                                    |       | PEIPKGR*GLF | PEIPKGR*GLF             | PEIPKGR*GLF | PEIPKGR*GLF             | PEIPKGR*GLF             | PEIPKGR*GLF            |
| НА       | Receptor binding site<br>(RBS)                   | T189A | Α           | Α                       | Α           | Α                       | Α                       | Α                      |
|          |  | Q226L | Q           | L                       | L           | L                       | L                       | L                      |
|          | (H3 Numbering)                                   | G228S | G           | G                       | G           | G                       | G                       | G                      |
| NA       | Stalk deletion                                   |       | 69-73       | 69-73                   | 69-73       | 69-73                   | 69-73                   | 69-73                  |
|          | Antiviral resistance                             | E120V | E           | E                       | Е           | E                       | E                       | E                      |
|          |  | H276Y | Н           | Н                       | Н           | Н                       | Н                       | Н                      |
|          |  | R294K | K           | R                       | R           | R                       | R                       | R                      |
| M1       | Increase virulence in mice                       | N30D  | D           | D                       | D           | D                       | D                       | D                      |
|          |  | T215A | А           | Α                       | Α           | А                       | Α                       | Α                      |
| M2       | Antiviral resistance                             | S31N  | N           | N                       | N           | N                       | N                       | N                      |
| NS1      | Increase virulence in mice                       | P42S  | S           | S                       | S           | S                       | S                       | S                      |

<sup>\*</sup> The numbering starts with the first condon of Methionine for these proteins accepts HA.

<sup>&</sup>amp; Strain of Wuxi/1 denoted for A/Wuxi/1/2013 was isolated from the daughter, Wuxi/2 denoted for A/Wuxi/2/2013 from the index patient, and Env/1 denoted for A/Environment/Wuxi/1/2013 from environmental sample of the live-poultry market where the index patient used to visit.

## **Definition of H7N9 cases and close contacts**

According to Chinese Guidelines for Diagnosis and Treatment of Human Infection with H7N9 Avian Influenza issued by the National Health and Family Planning Commission on April 2, 2013, laboratory-confirmed H7N9 cases were defined as patients with influenza-like illness symptoms as well as respiratory specimens that tested positive for H7N9 virus one of the following: isolation of H7N9 virus or positive results by real-time reverse transcription polymerase chain reaction (rRT-PCR) assay for H7N9, or a fourfold or greater rise in antibody titer for H7N9 virus based on testing of an acute serum specimen (collected 7 days or less after symptom onset) and a convalescent serum specimen collected at least two weeks later.

According to *Chinese Guidelines for Prevention and Control of Human Infection with H7N9 Avian Influenza* issued by the National Health and Family Planning Commission on April 3, 2013, a close contact was defined as: a) healthcare workers who provided medical service and family members who provided cares for suspected or confirmed H7N9 cases without effective personal protection; or b) any person who lived together or contacted within one metre with H7N9 cases during the period of one day before the case illness onset till to the case was isolated or died.